JMSCR Vol||04||Issue||04||Page 10140-10145||April 2016

www.jmscr.igmpublication.org

Impact Factor 5.244
Index Copernicus Value: 5.88
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i4.27

IGM Publication Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

A Fetal Study of Craniorachischisis, With Emphasis on Prenatal Diagnosis and Prevention

(Original Article)

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Abstract

Introduction: *Central nervous system (CNS) malformations constitute a sizeable percentage of the total incidence of the congenital malformations second only to cardiac malformations. Failure of fusion of cephalic part of neural tube is known as Exencephaly and caudal part of neural tube is Spina bifida.*

Aim: *This study was aimed at providing a comprehensive knowledge of Craniorachischis is which is characterized by anencephaly accompanied by open spina bifida. It was also associated with congenital fissure in the skull and vertebral column. This is the severe form of NTDs and recent evidences proves folic acid reduces the occurrence of NTDs 50-70% when taken periconceptionally. Therefore emphasis was based on prenatal diagnosis and prevention.*

Methods and Results: *The present study includes 1000 live births with 100 stillborn foetuses and abortuses to elucidate Craniorachischisis. The two unclaimed foetuses, one Craniorachischisis totalis and other being Craniorachischisis with omphalocele we resent from the department of Obstetrics and Gynecology. The detail Family and Obstetric history was not available.*

Discussion: *Neural tube defect (NTDs) is an embryonic induction disorder which results from failure of formation of both mesoderm and neuroectoderm. The reduction of 50-70% of NTDs following periconceptional folic acid administration initiated series of clinical studies by number of authors.*

Conclusion: *In conclusion most NTDs are sporadic and both genetic and non-genetic environmental factors are involved in its etiology.*

Keywords: *Craniorachischisis, Omphalocele, Neural tube defects (NTDs), Spina bifida and Anencephaly.*

Introduction

Central nervous system (CNS) malformations constitute a total incidence of the congenital malformations next to cardiac malformations. Neural tube defects can be classified as open if neural tissue is exposed or covered only by membrane and closed, if the defect is covered by normal skin. The Neurulation is normally completed within 28 days after conception, before many women are aware that they are pregnant. Disturbance of any of the sequential events of embryonic neurulation produces NTDs, with the phenotype Anencephaly or Spina bifida or both[1,2&3.]

Congenital anomalies are of greater interest to Anatomists, radiologists, obstetricians and paediatricians. The incidence of NTDs involving the brain or spinal cord or both is 0.5- 2 per 1000 pregnancies worldwide, and more common in females. Positive family history is an important risk factor and recurrence risk is 5% with previous affected child. Incidence of NTDs in India varies from 0.6 – 13/1000 births and varies in different population[4&5].

Craniorachischisis is a most severe form of neural tube defect characterized by anencephaly confluent with spina bifida open from cervical to lumbar or sacral region[6]. The present two unclaimed foetuses were delivered and both motherscame from economically poor background with probably folic acid deficiency and no prenatal care at all. The two foetuses were females, was sent to anatomy department. One was identified as Craniorachischisis totalis which was full term stillborn female and the other 26-28 weeks aborted female foetus with Craniorachischisis associated with omphalocele.

Materials and Methods

The study was carried out in a collection of 1000 live births with 100 stillborn foetuses and abortuses in the department of Anatomy over a period of two years. The two unclaimed Craniorachischisis babies were observed among the stillborn foetuses and abortuses. The detail study of these foetuses was done after fixing with formalin. However, dissection of foetuses was not carried out to find any internal abnormalities. Their findings were appropriately documented and photographed.

Observations and Results

The two fetuses were still born and aborted babies between 26 to 40 weeks presented with, Craniorachischisis (NTDs) (0.2%). The fetuses showed presence of Anencephaly with extension of defect to the spinal region i.e., Craniorachischisis. Both the fetuses were females and their findings were appropriately documented and photographed. The Internal dissection was not carried out.

1. **Craniorachischisis with omphalocele**

Fig1a & 1b (posterior & anterior view): Female Fetus around 26-28weeks presented with Craniorachischisis with associated omphalocele. The foetus showed absence of scalp, cranial vault which was extending up to upper thoracic vertebrae. The brain tissue and the spinal cord in the cervical and upper thoracic region were exposed. Below the level of upper thoracic region no defect was observed and vertebral column was covered by normal skin (Fig 1a).

The eyes were bulging with no neck and with extreme extension of head. It was also associated with a large omphalocele covered with amniotic membrane and placenta covered with membranes below the omphalocele on theanterior surface (Fig 1b).

2. **Craniorachischisis totalis (posterior view) Fig 2:**

The full term female fetus around 40weeks presented with Craniorachischisis totalis and spinal defect. The fetus presented with a defect in skull vault which extended up to lumbosacral region. The brain tissue and the spinal cord were exposed. In the caudal part of the spinal region the nerve rootlets were exposed to the exterior. It was associated with retro flexion of the spine. The neck was absent and the head seems to arise directly from the trunk. No other abnormalities were observed externally.

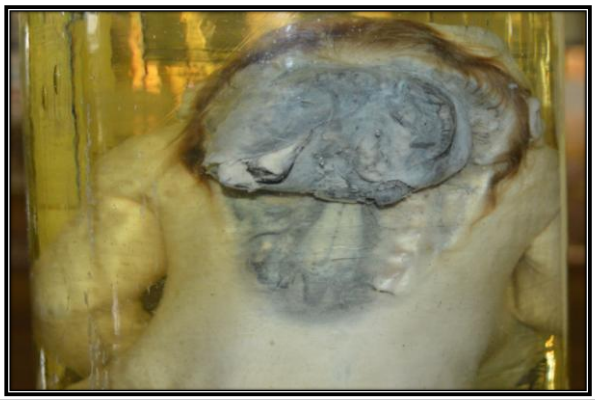

Fig 1a:Female Fetus(26-28weeks) showing Craniorachischisis associated with Omphalocoele (posterior view)

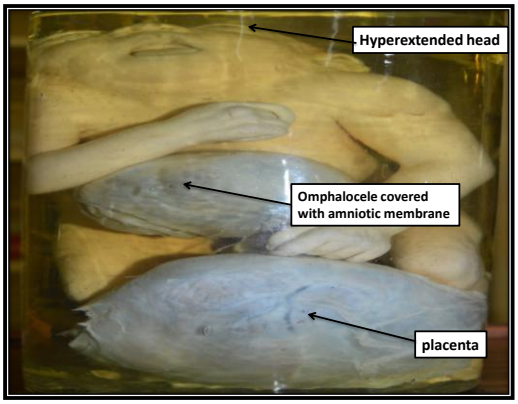

Fig 1b: Female Fetus (28 weeks) showing Craniorachischisis associated with Omphalocoele (anterior view)

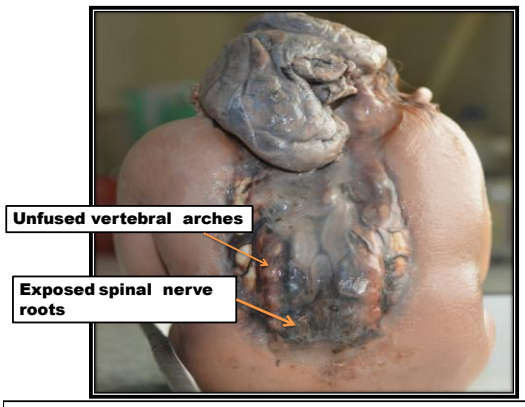

Fig 2: Female Full term Foetus showing Craniorachischisis Totalis with exposed spinal nerve rootlets most caudally.

Discussion

Neural tube defect (NTDs) is an embryonic induction disorder which results from failure of formation of both mesoderm and neuroectoderm. Craniorachischisisfoetuses often spontaneously abortduring pregnancy or expire soon after birth. It may be associated with other anomalies such as Omphalocele, Cardiac defects, caudal regression syndrome, hypoplastic lungand gastrointestinal atresia. Foetuses with neural tube defects involving the brain, lack functioning cerebrum which rules out the possibility of gaining consciousness. They are blind, deaf and unable to feel pain. Some foetuses may have rudimentary brainstem which controls the autonomic function[7,8&9].

Neurulation is broadly divided into two phases. The primary phase occurs in 3rd and 4th week of intrauterine life, which involves the formation of brain and spinal cord from cervical region up to the lumbar region. The secondary phase completes thesacral and coccygeal regions[10].Primary neurulation is associated with open NTDs including Anencephaly, open Spina bifida and Craniorachischisis. Secondary neurulation is associated with closed NTDs like spina bifida occulta[11, 12].

Primary neurulation has four distinctanatomical closure sites which forms multiple site neural tube fusion[13&14.]

1. First closure is at hindbrain/ cervical spine, and progresses both rostrally and caudally. Caudally it proceeds to the end of the neural groove until the caudal neuropore.
2. Second closure is at forebrain / midbrain boundary extends both rostrally and caudally and completes the roof of telencephalon and metencephalon.
3. Third closure site is at the end of forebrain and closes the rostral end of the neural groove closing the cranial neuropore.
4. The fourth site appears at the caudal end of the neural groove and extends rostrally to meet the fusion extending back from site one.

Phenotype of NTD will vary depending on the involvement of site of fusion[14].

Craniorachischisis is the most severe disorder of primary neurulation, clinically characterized by thecomplete absence of skull, defects in vertebrae and skin, results from failure of closure at sites 2, 4 and 1.

There are three types of anencephaly described[15]:

1. Meroanencephaly, where there is rudimentary brain tissue and partial formation of the cranium.
2. Holoanencephaly, the most common type, in which the brain is completely absent.
3. Craniorachischisis, the most severe, where defect extends beyond the cranium.

Number of authors hypothesized that folate related genes play an important role in the development of neural tube and inetiology of omphalocele. Insult to foliate genes pathways can lead to

abnormality in the midline developmental field. This leads to the combination of Craniorachischisis with omphalocele, diaphragm-tic defects, with cleft palate and cleft lip[7].

In the present study, one fetus had concomitant Craniorachischisisand omphalocele. Thus we can conclude that, there is high probability of severe maternal folic acid deficiency in relation to our fetus, however obstetric history was unavailable. Socioeconomic conditions have been thought to contribute to the risk of NTDs.

Johnson et al (2004) reported 16 cases of Craniorachischisis in a Texas Mexico border population[16].

In a study of 60 cases with omphalocele, Forrester and Merz found that 15% of the cases had NTDs, including 5% with anencephaly and 10% with spina bifida[7].

Kajarer et al (1994) investigated the axial skeleton is related to the notochord in human anencephalic fetuses. Abnormal ossification of cranial base was observed with or without cervical rachischisis[6].

NTDs overall have a female sex bias. Females more often than males tend to have Craniorachischisis, spina bifida involving the cervico-thoracic region, while males have spina bifida affecting the lumbosacral region[15].

In our study, the two foetuses were females with Craniorachischisis which obeys the trend.

Maternal hyperthermia in early pregnancy, during critical periods of gestation is associated with increased risk for neural tube defects, particularly the brain is very sensitive and hyperthermia may be a human teratogen[17].

NTDS is multifactorial. Exposure to valproic acid (antiepileptic drug), metabolites and toxins like lead during the critical period of gestation interferes with normal foliate metabolism and increases the likelihood of NTDs. Therefore women taking anti-epileptic drugs during pregnancy are advised to undergo routine antenatal check-up with Alpha feto protein[18].

Cyclophosphamide is a strong inhibitor of DNA synthesis resulting in antiproliferative activity of axial mesoderm leading to axial skeletal malformationsmay result in skull vault and vertebral defects[1].

A study was conducted and published regarding maternal preconceptional smoking and alcohol consumption on the risk of NTDs. Maternal alcohol increases the risk of NTDs whereas smoking was associated with low risk of NTDs. These observations are elusive[9].

NTDs may be associated with the unbalanced form of a structural chromosomal abnormality in some families. NTDs results from genetic factors, probably at more than one locus, interacting with environmental and dietary factors. Consanguinity was suggested to contribute to the high incidence of NTDs.

Many genes are required for neuralization, expression and specific pathways. The genes which encode and disrupt NTDs include *Hectd1*, *Mib2 and Smurf1/2*. These proteins function as signalling pathways for neural tube closure. The mutations of genes involved in folic acid metabolism are genetic risk factors for the recurrence of NTDs[19, 20, 21].

The reduction of 50-70% of NTDs following periconceptional folic acid administration initiated series of clinical studies by number of authors. This suggested that genes correlated with folate and methionine metabolism can be involved in the etiology of NTDs. The NTDs reduced by intake of folic acid and vitamin B12 during preconception and regular maternal counseling[21,22,23].

In the current study, we noted one of the Craniorachischisis was associated with omphalocele and the second case was Craniorachischisis Totalis with caudal exposure of spinal nerve rootlets. Genetic analysis for associated structural chromosomal abnormalities was not done in these foetuses related families, since both family and obstetric history were not collected as they never came for antenatal check-ups and follow up. But both mothers belong to low socioeconomic conditions which may be the etiological factor for Craniorachischisis.

Conclusion

Craniorachischisisare severe congenital anomalies associated with various detrimental clinical features and continues to provide multifaceted challenge to Anatomists, Epidemiologists and Clinicians. The prognosis of Craniorachischisis defects is exceptionally poor and death of the neonate is unavoidable. Craniorachischisis are anomalies that can be detected in 6-10 gestational weeks period by high resolution MRI. Our imminent eradication was predicted by prenatal diagnosis by screening for AFP, US G and MRI. The rapid preventive effect of taking folic acid and vitamin B12 supplementation during periconceptional stage is well proved in preventing many birth defects including NTDs worldwide.

It is my hope that these foetuses will stimulate lively discussion and give all of us an opportunity to learn something new about these rare disorders.

Conflict of interest

All authors have none to declare

Acknowledgements

All authors are thankful to Department of Obstetrics and Gynecology for providing us the foetuses with the rare anomalies. Authors of this study are grateful to, editors and publishers of all those articles, journals and books from where literature for this article has been reviewed and discussed.

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